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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,038	06/14/2001	Olivier Meyer	032751-049	7218

7590 01/15/2003  
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EXAMINER
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ANGELL, JON E

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 01/15/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/880,038

Applicant(s)

MEYER, OLIVIER

Examiner

J. Eric Angell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 October 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 22-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. This Action is in response to the communication filed on 10/30/02, as Paper No. 8.  
Claims 1-26 are pending in the application and are addressed herein.

#### ***Election/Restrictions***

2. Applicant's election with traverse of Group I (claims 1-21) and of the species: Hexadecylphosphocholine (HPC) and IL-2 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that applicants do not believe that the search required for the additional Group would be burdensome. This is not found persuasive because as mentioned in the previous Office Action, the Groups have different classifications, prima facie evidence of a burdensome search.

The requirement is still deemed proper and is therefore made FINAL.

The prior art does not appear to anticipate, nor make obvious the claimed complex comprising the elected species (HPC). Therefore, following the rules pertaining to species elections, the next species considered is a complex comprising Dipalmitoylphosphatidylcholine.

#### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (WO 99/05303; published 4 Feb. 1999) in view of Addison et al. (Gene Therapy 1998, 5:1400-1409).

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Zhang teaches a combination product comprising a nucleic acid and a phospholipid (Dipalmitoylphosphatidylcholine) for delivering the nucleic acid of interest to a cell in a subject for therapeutic purposes. Zhang does not specifically teach that the phospholipid has cytotoxic activity; however, looking to the specification for guidance, any phospholipid having the general structure set forth in the general formula (A) on page 11 of the specification, would necessarily have a cytotoxic effect. The phospholipid taught by Zhang (Dipalmitoylphosphatidylcholine) is encompassed by the phospholipid of general formula (A) (p. 11 of the specification). Therefore, the phospholipid taught by Zhang would necessarily have cytotoxic activity. Furthermore, Dipalmitoylphosphatidylcholine as a compound meets the limitations of claims 2-7, considering the claims are drawn to a molecule wherein R1 comprises 6-22 carbon atoms, etc. It is noted that the R1 group of Dipalmitoylphosphatidylcholine comprises at least 22 carbon atoms.

Zhang teaches that the complex can comprise a cationic lipid which associates with the nucleic acid (see p. 3, lines 7-16) and a cholesterol (a lipid which is capable of integrating into the phospholipid) (see p. 10, lines second paragraph). Zhang teaches that the nucleic acid, phospholipid as well as the cationic lipid can form a complex (see page 15, third paragraph). Zhang also indicates the non-cationic lipid can be present at a concentration in the range of about 20 to about 95 mole percent, while the cationic lipid concentration can be in the range of about 5 to about 80 mole percent and the PEG-lipid concentration can be between 0.5 to 50 mole percent (see p. 15, third paragraph). Therefore, Zhang teaches possible ranges for the positive and negative charges such that the concentrations could be adjusted such that the ratio of positive to negative charges of the elements forming the complex ranges between 0.05 and 20.

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Zhang teaches that the lipid-nucleic acid complex is typically in the range of 200-500 microns (see p. 17, fourth paragraph).

Zhang also indicates that the lipid-nucleic acid complex can be hydrated in a pharmaceutically acceptable buffer such as HEPES or PBS (see p. 17, third paragraph).

Although Zhang teaches that the nucleic acid of the complex can be a DNA such as plasmid DNA (see abstract) Zhang does not specifically teach that the nucleic acid encodes a cytotoxic polypeptide, such as IL-2.

However, Addison teaches an adenoviral vector which expresses IL-2. When the adenoviral IL-2 vector is delivered to a tumor in a mouse, it results in tumor regression (e.g. see abstract or p. 1402, Table 1). Therefore, Addison teaches that the adenoviral IL-2 vector is useful for causing a cytotoxic effect in tumor cells.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the complex product taught by Zhang by substituting the adenoviral-IL-2 vector taught by Addison for the nucleic acid, thus create a combination product comprising a nucleic acid encoding a cytotoxic polypeptide and a cytotoxic phospholipid (as indicated above) with a reasonable expectation of success.

The motivation to combine the references is provided by Zhang who teaches "the lipid-nucleic acid particles of the present invention have enhanced circulation characteristics and serum stability and, thus, they are extremely effective as a nucleic acid delivery system." (See abstract).

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell  
January 13, 2003

  
DAVE T. NGUYEN  
PRIMARY EXAMINER